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EXAMINER	
EPPERSON, JON D	
ART UNIT	PAPER NUMBER
1639	14

DATE MAILED: 05/30/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
File Copy	09/742,033	SUN ET AL.	
	Examiner	Art Unit	
	Jon D Epperson	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 February 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *3,4,9-20,22 and 26-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,4,9-20,22 and 26-34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Please note: The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1639.

Status of the Application

1. The Response filed February 27, 2003 (Paper No. 13) is acknowledged.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

3. As an initial matter, Applicants argue that the "Examiner's refusal to consider and respond to Applicant's arguments set forth in their Preliminary Amendment is improper. Applicants prepared and submitted the Preliminary Amendment to address rejections raised in the parent application [i.e., the present application is a continuation of serial number 08/936,971 now abandoned as of September 21, 2000] and to further prosecution of the present continuation application." Applicants further rely on MPEP § 707.07(f) to support their arguments:

> Where the requirements are traversed, or suspension thereof requested, the examiner should make proper reference thereto in his or her action on the amendment. **Where the application traverses any rejection, the examiner should, if he or she repeats the rejection, take note of the applicants' argument and answer the substance of it**. If a rejection of record is to be applied to a new or amended claim, specific identification of that ground of rejection, as by citation of the paragraph in the former Office letter in which the rejection was originally stated, should be give.

[MPEP § 707.07(f), emphasis added].

4. The Examiner does appreciate Applicants arguments, but does not believe that the MPEP § 707.07(f) applies in this case. It is the Examiner's position that this is a "new" application wherein prosecution is not continued from a previous application like an RCE, but has essentially started over. Consequently, the Examiner does not need to address arguments that pertain to rejections in a parent case although they have been fully considered in this case (i.e., the Examiner is not bound to the prosecution in the parent case) because those rejections were not made in this case (at least not as of the time of Applicant's January 26, 2001 amendment and, as a result, the Examiner is not "repeating" a rejection because no rejection had yet been made in this "new" case as of Applicant's January 26, 2001 amendment and "Response"). Furthermore, Applicants have added new claims and, as a result, the rejections could not have been "repeated" because they now apply to a different set of claims that were not present in the parent case and hence are "new" rejections.

Status of the Claims

5. Claims 3-4 and 9-22 were pending in the present case. Applicant amended claims 3-4, deleted claim 21 and added claims 26-34. Consequently claims 3-4, 9-20, 22 and 26-34 are currently pending.

6. This application contains claims (e.g., claims 23-25) drawn to inventions nonelected with traverse in Paper No. 11). This was addressed in the previous action. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144). See MPEP § 821.01.

Priority Claims

7. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

Applicant's claim for domestic priority under 35 U.S.C. 120 is acknowledged. However, the applications upon which priority is claimed fail to provide adequate support under 35 U.S.C. 112 for the claims of this application. In the instant case, applicant's admit that claims 9, 11 and 14-17 are "apparently not supported by the disclosure of the other priority applications" (see Paper No. 13, page 5, paragraph 3). Consequently, the generic claims to which claims 9, 11 and 14-17 must also not be fully supported because those claims would encompass the compounds disclosed in claims 9, 11 and 14-17. Furthermore, all of the claims that subsequently depend on these unsupported generic claims would also not be adequately supported including claim 17 (please note that *ipsisima verba* support is not the test for possession). Therefore, the priority of the claims is the date of the parent case 08/936,971 or **September 25, 1997** as stated in the previous Office Action.

Withdrawn Objections/Rejections

6. The objection to figure 1 is hereby withdrawn in view of Applicants corrections. The objections to the oath and/or declaration is hereby withdrawn. The rejections (written description and enablement) under 35 USC 112, first paragraph, are hereby withdrawn (in part) to claim 9 only for both the written description and enablement (the rejections for written description and enablement are hereby maintained with regard to all other claims, see below).

The rejection under 35 U.S.C. § 102(g) over '581 is hereby withdrawn in view of Applicants arguments. All other rejections are maintained and the arguments are addressed below.

Outstanding Objections and/or Rejections

8. Claims 3-4 and 10-20, 22, and 26-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

To satisfy the written description requirement, an applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. Applicant's claims are directed to compounds, which comprise "an electrochemiluminescent label linked to a coreactant, such that said compound emits electrochemiluminescence when exposed to electrochemical energy." In this case, applicants have not provided enough examples to demonstrate that they are in possession of the full scope of the invention as claimed. For example, it is not possible to know which ECL/CR pairs will have sufficient energy and react with sufficient speed (i.e., favorable reaction kinetics) *a priori* to produce the necessary electronically excited products. While, determining the free energy for a given set of Acceptor/Donor species may provide an answer for a limited number of ECL/RC pairs via a calculation of the standard electrochemical potentials i.e., $\Delta G^0 = E^0(A/A-)-E^0(D+/D)$ where A is an acceptor and D is a donor species (see specification, page 12), the specification does not provide teachings for more complicated reactions. For example, applicants' claims

would also encompass energy-deficient systems that generate light emission via triplet-triplet annihilation. Applicants have not provided any "formula" for calculating which ECL/RC pairs would fall under this category and since applicants do not "wish to be bound by a theoretical explanation of reaction mechanism" (see specification, page 11, lines 1-2), more complicated reactions of this type would be encompassed by the claims. Furthermore, applicants have not provided sufficient guidance to determine what structural features of a given ECL/RC pair that would insure the favorable reaction kinetics that are required for these type of reactions or which ECL/RC pairs would demonstrate the required stability. Therefore, it is not clear which compounds fall within the scope of applicant's claims and, as a result, applicant cannot be in possession of the full scope of the invention.

Furthermore, Applicants' claims encompass a broad genus. For example, claim 3 is drawn to a compound that comprises an electrochemiluminescent "label" linked presumably by a "linker" to a "coreactant" such that the compound emits electrochemiluminescence when exposed to electrochemical energy. The scope of this claim includes an infinite number of compounds wherein no distinguishing structural attributes are provided for the "label", "linker" or "coreactant." The specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form the label, linker and coreactant. Furthermore, the specification and claims do not provide ***any*** guidance as to what structural features ***all*** of these electrochemiluminescent compounds share. Consequently, it is not possible to determine *a priori* which compounds would encompass because there is no common structural attributes that can link together ***all*** of these potential compounds i.e., there is no teaching that would allow a person of skill in the art to determine *a priori* ***all*** the different

types of labels, linkers and coreactants that should be included in this genus from the few examples provided by applicants.

The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Furthermore, the general knowledge and level of skill in the art are not developed enough to provide sufficient guidance to supplement the deficiencies in the description particularly for "energy-deficient" systems (i.e., wherein the compounds generate electrochemiluminescence via a triplet-triplet annihilation pathway, see above, which would be encompassed by Applicants broad claims) because there are simply no theories known that would allow a person of skill in the art *a priori* to determine whether a compound would or would not generate electrochemiluminescence via a triplet-triplet pathway simply by looking at its structure or by calculating standard electrochemical potentials i.e., $\Delta G^0 = E^0(A/A-)-E^0(D+/D)$ where A is an acceptor and D is a donor species (note: compounds that operate via the triplet-triplet mechanism would fail this test because they are "energy deficient" and hence a simple calculation of the ΔG^0 would not provide an answer as to whether these compounds would or would not emit electrochemiluminescence upon oxidation/reduction via ECL, see also Applicants' specification, page 12; however, this does not mean as purported by Applicants that these compound lack the energy to emit electrochemiluminescence when exposed to electrochemical energy). Since the disclosure fails to describe the common attributes or characteristics that identify ***all*** of the members of the genus or even a substantial portion thereof, and because the genus is enormous and highly variant, listing examples like tris-bipyridines conjugated to various amino acids and the variations listed on pages 13-14 (see specification, Examples; see also figures 1-2; see also specification pages

13-14) is insufficient to teach the entire genus. Consequently, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe this enormous genus.

Additionally, it is not possible to determine the limit of compounds that fall within the scope of these claims because the term "coreactant" encompasses "species which are capable of undergoing a chemical transformation to form said interactive species or said precursor species", which would read on all compounds (given an infinite number of chemical transformations).

As a result, applicants have not demonstrated in "full, clear, concise, and exact terms" that they are in possession of the full scope of the claimed invention.

With respect to adequate disclosure of the scope of the presently claimed generic applicant is referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding disclosure. For adequate disclosure, like enablement, requires *representative examples*, which provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that *applicant had possession of the full scope of the claimed invention*. See *In re Riat* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and *University of California v. Eli Lilly and Co* cited above (for disclosure). Therefore it is deemed that the disclosure is neither representative of the claimed genus, nor does it represent a substantial portion of the claimed genus since the applicant has not disclosed ***enough*** specific examples of the elected invention. Moreover, the claimed genus encompasses members, which are yet to be prepared or envisioned.

Response to Arguments

9. Applicant's arguments have been fully considered but they are not found persuasive. The examiner's rationale is set forth below. Please note that the above rejection has been modified to address Applicants' arguments and/or amendments and/or to include Applicants' newly added claims.

10. Applicant argues that **[1]** the claims "cannot encompass "energy deficient systems" or non-functional ECL emitter/coreactant pairs ... Therefore, the claims explicitly exclude compounds, which are "energy deficient" or do not produce ECL" (see page 7, paragraph 3), **[2]** the "absence of 'enough examples' is not relevant to a determination of compliance with the "written description requirement" of the first paragraph ... [because] Examples are not required (see page 7, paragraphs 3-4 outlining test for written description), **[3]** there is no reasonable basis to assert that the claims must be limited to the specific species and that the specific $Ru(bpy)_3^{2+}$-TPA pair disclosed in the specification is provided only as an example and that the original specification broadly describes the terms "electrochemiluminescent label" and "coreactant" on page 6 and discloses an extensive list of useful pairs on pages 13-14. Applicant further cites Reagents of the University of California v. Eli Lily, 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed Cir. 1997) stating, "in claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed

genus" (see page 8, paragraph 1), **[4]** it is unclear what is the basis for the alleged rejection that 'it is not possible to determine the limit of compounds that fall within the scope of these claims because the terms 'coreactant' encompasses 'species which are capable of undergoing a chemical transformation to form said interactive species or said precursor species' and that "Applicants urge that the claim limitations are clear and definite when properly construed in view of the specification" (see page 8 paragraph 2), **[5]** and that claims 3 and 4 have been amended to specify that the coreactant is a material that is oxidized to produce a reductant, or reduced to produce an oxidant.

Applicants' arguments have been fully considered but are not found persuasive for the following reasons:

The Examiner contends that **[1, 3, 4]** the term "energy-deficient" systems does not mean "compounds that do not have enough energy to produce ECL" as purported by Applicants. Rather, the "energy-deficient" term refers to ECL emitter/coreactant pairs that "generate light emission via triplet-triplet annihilation" (see original rejection, paper No. 11, paragraph 9; see also Faulkner, L. R., pages 500-502, especially figure 2 and last paragraph on page 501, "light emission from energy-deficient systems is usually rationalized via a mechanism involving triplet intermediates ... [wherein] two of the triplets can undergo triplet-triplet annihilation" wherein the Faulkner reference is being cited herein solely for the purpose of refuting Applicants' arguments).

The point here is that as stated in the modified rejection above, these claims encompass a broad genus. For example, claim 3 is drawn to a compound that comprises an electrochemiluminescent "label" linked presumably by a "linker" to a "coreactant" such that the

compound emits electrochemiluminescence when exposed to electrochemical energy. The scope of this claim includes an infinite number of compounds wherein no distinguishing structural attributes are provided for the "label", "linker" or "coreactant." The specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form the label, linker and coreactant. Furthermore, the specification and claims do not provide ***any*** guidance as to what structural features ***all*** of these electrochemiluminescent compounds share. Consequently, it is not possible to determine *a priori* which compounds would encompass because there is no common structural attributes that can link together ***all*** of these potential compounds i.e., there is no teaching that would allow a person of skill in the art to determine *a priori* ***all*** the different types of labels, linkers and coreactants that should be included in this genus from the few examples provided by applicants.

The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Furthermore, the general knowledge and level of skill in the art are not developed enough to provide sufficient guidance to supplement the deficiencies in the description particularly for "energy-deficient" systems (i.e., wherein the compounds generate electrochemiluminescence via a triplet-triplet annihilation pathway, see above, which would be encompassed by Applicants broad claims) because there are simply no theories known that would allow a person of skill in the art to determine *a priori* whether a compound would or would not generate electrochemiluminescence via a triplet-triplet pathway simply by looking at its structure or by calculating standard electrochemical potentials i.e., $\Delta G^0 = E^0(A/A-)-E^0(D+/D)$ where A is an acceptor and D is a donor species (note: compounds that operate via the triplet-triplet mechanism would fail this test because they are

"energy deficient" and hence a simple calculation of the ΔG^0 would not provide an answer as to whether these compounds would or would not emit electrochemiluminescence upon oxidation/reduction via ECL, see also Applicants' specification, page 12; however, this does not mean as purported by Applicants that these compound lack the energy to emit electrochemiluminescence when exposed to electrochemical energy; please also note that this does not even include the myriad of other factors that would also need to be considered including stabilization of radical donor/acceptor pairs, competing oxidation/reduction reactions, steric hindrance, etc.). Since the disclosure fails to describe the common attributes or characteristics that identify ***all*** of the members of the genus or even a substantial portion thereof, and because the genus is enormous and highly variant, listing examples like tris-bipyridines conjugated to various amino acids and the "potential" variations listed on pages 13-14 (see specification, Examples; see also figures 1-2; see also specification pages 13-14) is insufficient to teach the entire genus. Consequently, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe this enormous genus.

Additionally (as stated in the above rejection), it is not possible to determine the limit of compounds that fall within the scope of these claims because the term "**coreactant**" encompasses "species which are capable of undergoing a chemical transformation to form said interactive species or said precursor species", which **would read on all compounds (given an infinite number of chemical transformations)**. Consequently, applicants' assertion **[4]** that it "is unclear what is the basis for the alleged rejection that 'it is not possible to determine the limit of compounds that fall within the scope of these claims because the terms 'coreactant' encompasses 'species which are capable of undergoing a chemical transformation to form said

interactive species or said precursor species' and that "Applicants urge that the claim limitations are clear and definite when properly construed in view of the specification"" is not found persuasive because the Examiner has set forth a clear reason why it is not possible to determine what compounds fall within the scope (see underlined reasoning above in this paragraph i.e., that coreactant would read on all compounds given an infinite number of chemical transformations) and Applicants have not provided any rationale as to how or why the claim limitations would be clear and definite in view of the specification other than to say that they are without providing any rationale or proof. Therefore, the Examiner has **[3-4]** provided a "reasonable basis" for asserting that Applicants are not in possession of the full scope of the claimed invention.

With regard to the number of examples provided by Applicants, the Examiner contends that **[2]** with respect to adequate disclosure of the scope of the presently claimed generic applicant is referred to the discussion in *University of California v. Eli Lilly and Co.* (U.S. Court of Appeals Federal Circuit (CAFC) 43 USPQ2d 1398 7/22/1997 Decided July 22, 1997; No. 96-1175) regarding disclosure. For adequate disclosure, like enablement, requires ***representative examples*** that provide reasonable assurance to one skilled in the art that the compounds falling within the scope both possess the alleged utility and additionally demonstrate that ***applicant had possession of the full scope of the claimed invention***. See *In re Riat et al.* (CCPA 1964) 327 F2d 685, 140 USPQ 471; *In re Barr et al.* (CCPA 1971) 444 F 2d 349, 151 USPQ 724 (for enablement) and University *of California v. Eli Lilly and Co* cited above (for disclosure). The more unpredictable the art the greater the showing required (e.g. by "representative examples") for both enablement and adequate disclosure.

Finally, the Examiner contends that Applicants amendments **[5]** do not in any way resolve the issues set forth above because the claims are still drawn to a broad genus that encompasses an infinite number of compounds with undefined and undeterminable structure as set forth above and, as a result, a person of skill in the art would conclude that Applicants are not in possession of the full breadth of the claimed invention.

Accordingly, the written description rejection cited above is hereby maintained.

11. Claims 3-4 and 10-20, 22, and 26-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific metal-tris-terpyridine complexes linked tertiary amines disclosed, does not reasonably provide enablement for ***any*** electrochemiluminescent "label" linked via ***any*** "linker" to ***any*** "coreactant." The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use invention as broadly as it is claimed. This is an enablement rejection.

The claims are directed toward a product which is a compound comprised of an ECL label linked to a coreactant. The disclosure teaches a number of specific coreactants including various tertiary amines and ECL labels comprised of $Ru(by)_3$. However, does not provide enablement for any compound comprised of any label, linker and coreactant. For example, the preparation and use of coreactants which are present as precursors or species which can be transformed into a coreactant coupled to a generic ECL label does not appear to be within the scope of reasonable experimentation. The factors to be considered in a determination of undue experimentation are disclosed in *In re Wands*, (U.S.P.Q. 2d 1400 (CAFC 1988)). The factors to

be considered include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the predictability of the art and the breadth of the claims.

A number of factors would prevent one of skill in the art from practicing the invention without undue experimentation, these are summarized as follows:

1) The specification fails to give adequate direction and guidance as to all of the reactions which may be used to transform a compound into a reactive species or which precursors are useful. Moreover, the specification does not teach how to prepare such coreactant compounds, the specifics of the stability or the use. In addition the specification teaches limited ECL labels, specifically OS or $Ru(byp)_3$ and some Ru pyridine complexes.

2) Applicants have provided limited working examples and/or teachings not commensurate in scope with the broad recitations of a "coreactant" or an "ECL label." There are also no examples of the complexes of ECL labels linked to coreactants commensurate in scope with the broad claims.

3) The breadth of the claims encompasses an indefinably large number of compounds as it is unclear what is and is not transformable into an interacting species and hence what is a coreactant. The breadth of the claims also sets forth any ECL label to which any of the indefinably large number of compounds will have to be linked to and remain functional. For example, claim 3 is drawn to a compound that comprises an electrochemiluminescent "label" linked presumably by a "linker" to a "coreactant" such that the compound emits electrochemiluminescence when exposed to electrochemical energy. The scope of this claim includes an infinite number of compounds wherein no distinguishing structural attributes are

provided for the "label", "linker" or "coreactant." The specification and claims do not place any limit on the number of atoms, the types of atoms, or the manner in which said atoms might be connected to form the label, linker and coreactant.

4) The state of the prior art is such that a number of compounds that might be useful as coreactants have been prepared and even linked to ECL labels.

5) The art is inherently unpredictable because it is not possible to know *a priori* which coreactant, especially those requiring transformation to form a potentially interacting species will be transformable when linked to an ECL label and actually function as predicted with an undefined series of undisclosed ECL labels. Moreover, it is not possible to know *a priori* which complexes will be capable of preparation, stable prior to use yet function under undisclosed assay conditions in the ECL assay. The reason that it is not possible to know these conditions *a priori* is because it is not possible to know which ECL/RC pairs will have sufficient energy and react with sufficient speed (i.e., favorable reaction kinetics) *a priori* to produce the necessary electronically excited products. While, determining the free energy for a given set of Acceptor/Donor species may provide an answer for a limited number of ECL/RC pairs via a calculation of the standard electrochemical potentials i.e., $\Delta G^0 = E^0(A/A-)-E^0(D+/D)$ where A is an acceptor and D is a donor species (see specification, page 12), the specification does not provide enablement for more complicated reactions. For example, applicants' claims would also encompass energy-deficient systems that generate light emission via triplet-triplet annihilation. Applicants have not provided any "formula" for calculating which ECL/RC pairs would fall under this category and since applicants do not "wish to be bound by a theoretical explanation of reaction mechanism" (see specification, page 11, lines 1-2), more complicated reactions of this

type would be encompassed by the claims. Furthermore, applicants have not provided sufficient guidance to determine what structural features of a given ECL/RC pair would insure the favorable reaction kinetics that are required for these type of reactions. Furthermore, many other unpredictable factors would also play a role including stabilization of radical donor/acceptor pairs, competing oxidation/reduction reactions, steric hindrance.

Therefore, while it is true that the level of skill in the art is high (references like Knight et al are not enough to enable the broad scope of the present claims), it would still require undue experimentation to make and use the coreactant-ECL label complexes commensurate in scope with the invention claimed in the absence of guidance from the applicant as set forth above.

Response to Arguments

12. Applicant's arguments have been fully considered but they are not found persuasive. The examiner's rationale is set forth below. Please note that the above rejection has been modified to address Applicants' arguments and/or amendments and/or to include Applicants' newly added claims.

13. Applicant argues that **[1]** "it is improper to reject claims on the ground that the specification does not support the claims when the terms are no broader than the broadest description of the invention in the specification and there is no challenge to the operativeness of the subject matter embraced by the claims ... [and] the Examiner has the initial burden of establishing a reasonable basis to question the enablement provided for the claimed invention ... [and] that the Examiner has failed to provide any evidence or reasoning substantiating the

allegation that the presently claimed subject matter is not enabled. Accordingly, the burden of providing enablement has not shifted to the Applicant (see page 10, paragraph 1), **[2]** the relative skill in the art is high as demonstrated in part by the references cited in the specification including US Patent Nos. 5,310,687 and 5,643,713 (see pages 10-12) and a reference in the *Analyst* by Knight et al (see page 11, paragraphs 2-3), **[3]** that "enablement is not precluded even where the disclosure requires some experimentation" and because the level of skill in the art is high, "the threshold point at which experimentation becomes undue must also be high. Given this, Applicants submit that, based on the instant specification, one skilled in the art would not have to engage in undue experimentation", **[4]** "as long as the specification discloses at least one method for making and using the claimed invention that bears a reasonable correlation to the entire scope of the claim, the enablement requirement is satisfied ... Accordingly, Applicants respectfully submit that additional examples of the complexes of ECL labels linked to coreactants are not necessary" (see page 13, last three paragraphs.

14. The Examiner's position is that **[1]** a prima facie case has been established by the Examiner using the Wands factors set forth in the rejection above which constitutes the Examiners evidence and/or reasoning in point by point notation outlining why the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention as broadly as it is claimed.

Furthermore, the Examiner contends that **[2]** the level of skill in the art is only but one factor to consider using the *Wands* analysis and a person of skill in the art would conclude that Applicants were not enabled for the full scope of the claimed invention because the majority of

Wands factors (see above) do not favor Applicants position. Furthermore, the Knight et al reference (Knight et al "Occurrence, Mechanism and Analytical Applications of Electrogenerated Chemiluminescence", Analyst, 119, 879 (1994)) mentioned in Applicants' response (see page 11, paragraph 1) does not provide any teachings that would encompass the broad scope of Applicants' claimed invention wherein the "label", "linker" and "coreactant" could be virtually anything (i.e., reads on an infinite number of possibilities). The Knight et al reference discloses only a few aromatic hydrocarbons and metal-ligand complexes (see Knight et al, Table 1). Furthermore, a later reference by Knight et al (see Knight, A. W.; Greenway, G. M. "Relationship between structural attributes and observed electrogenerated chemiluminescence (ECL) activity of tertiary amines as potential analytes for the tris(2,2-bipyridine)ruthenium(II) ECL reaction" Analyst **1996**, 121, the reference is put forth for the sole purpose of refuting Applicants arguments) shows just how difficult it can be to "predict" which compounds will act favorably as a coreactant in an ECL reaction even when a much narrower class of compounds is considered (i.e., $Ru(bpy_3)^{2+}$ complexed to various amines). Although the reference points to some general guidelines for determining possible coreactants, the reference does not conclude that this area can be predicted with any degree of certainty stating only that "it is hoped that by consideration of these general conclusions, the reasons for the often diverse ECL activities observed for seemingly similar compounds can be further explained" (emphasis on the word "hoped") (see Knight et al, 101R, second column, last paragraph, "It is not the case, however, that all tertiary amine compounds take part in ECL reactions with $Ru(bpy)_3^{2+}$ to produce light. Many tertiary amine compounds produce intense emissions whereas other structurally related similar compounds produce virtually no ECL emission."). Consequently, the Examiner's

position is that if it is difficult if not impossible to predict what compounds would act favorably in ECL reactions for this narrow class of compounds (i.e., $Ru(bpy)_3^{2+}$ with tertiary amines) it certainly would be impossible to predict with any degree of certainty the infinite number of diverse compounds that are currently being claimed by Applicants.

Furthermore **[3]**, the Examiner is unaware of a legal precedence that states that a high level of skill in the art necessarily leads to a higher threshold for "undue" experimentation especially when the art includes areas that are "unpredictable" as set forth above. Furthermore, the issue here is not whether the level of skill in the art is high, but whether the claimed ECL compounds are sufficiently diverse that one of ordinary skill would not be able to make and use said ECL compounds that would fall within the scope of Applicants' broad claims. Here, the Examiner contends that Applicants claims read on an infinite number of compounds comprising a "label", "linker" and "co-reactant" with undefined structures and, as a result, one of skill in the art would not know how to make and/or use the vast majority of compounds that would fall within the scope of these broad claims.. Again note that the disclosure of the specification must be commensurate in scope with what is claimed. The issue here is the breadth of the claims in light of the predictability of the art as determined by the number of working examples, the skill level of the artisan and the guidance presented in the instant specification and the prior art of record. See the decisions in *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970), *Amgen v. Chugai Pharmaceuticals Co. Ltd.*, 13 USPQ2d, 1737 (1990), and *In re Wands*, 8 USPQ2d, 1400 (CAFC 1988). *In re Wands* stated that the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of

working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and, (8) the breadth of the claims. All of these factors were addressed in the initial rejection. *In re Fisher,* 427 F.2d 833, 166 USPQ 18 (CCPA 1970), held that

> "Inventor should be allowed to dominate future patentable inventions of others where those inventions were based in some way on his teachings, since such improvements while unobvious from his teachings, are still within his contribution, since improvement was made possible by his work; however, he must not be permitted to achieve this dominance by claims which are insufficiently supported and, hence, not in compliance with first paragraph of 35 U.S.C. 112; that paragraph requires that scope of claims must bear a reasonable correlation to scope of enablement provided by specification to persons of ordinary skill in the art; in cases involving predictable factors, such as mechanical or electrical elements, a single embodiment provides broad enablement in the sense that, once imagined, other embodiments can be made without difficulty and their performance characteristics predicted by resort to known scientific law; in cases involving unpredictable factors, such as most chemical reactions and physiological activity, scope of enablement varies inversely with degree of unpredictability of factors involved." (emphasis added)

If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. The examiner maintains for the reasons stated above that the art is unpredictable because it encompasses such an infinite number of diverse compounds and a person of skill in the art would not know how to make all of these diverse compounds and/or use these compounds when it is not even clear how to make and/or use a small subset (see above arguments for Wands factors) of these compounds and, as a result, the instant disclosure is not enabling for the full scope of the claims.

Finally **[4]**, for the reasons stated above and for the reasons presented in the rejection of record the Examiner maintains that the specification does not provide any examples and/or teachings that would enable the "entire scope" of the claimed invention.

Accordingly, the Enablement Rejection cited above is hereby maintained.

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

15. Claims 3-4, 9-20, 22 and 26-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 3-4, 9-20, 22 and 26-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 3-4, 9-20, 22 and 26-34 and/or depend on claims that recite a "coreactant" term. However, the definition of a coreactant on page 6 includes both precursor species and species which are capable of undergoing transformation to form interactive species. In view of he foregoing, the claim is vague and indefinite because it is not possible to determine which components are, or are not, coreactants and what processes or transformations are being conducted. Hence, it would not be possible to know if one had infringed the instant claims when generating a

compound which has an ECL label attached to any other molecule, as it would be unclear what process the attached molecule might be subject to that may transform it into a coreactant. Therefore, it is not possible to determine the metes and bounds of the invention as claimed.

B. Withdrawn.

C. Withdrawn.

D. Claim 22 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 22 recites a coreactant that is a species capable of interacting with said electrochemical luminescent label to produce electrochemiluminescence or a precursor species that upon exposure to electrochemical energy is transformed into a species that are capable of interacting with said electrochemical label to produce electrochmiluminescence. This is vague and indefinite as it is not clear what compounds will meet these limitations. Therefore, it is not possible to determine the metes and bounds of the invention as claimed.

Response

16. Applicant's arguments directed to the above 35 USC 112, second paragraph rejections were considered but were not deemed persuasive for the following reasons. Please note that the above rejections have been modified from their original to more clearly address applicants' newly amended and/or added claims and/or arguments.

For ***paragraph A***, Applicant argues that "the definition of 'coreactant' on page 6 is limited to reactants that can be linked to an ECL label to form an ECL compound that emits ECL when exposed to electrochemical energy. Moreover, the description of co reactant of page 6 is also supplemented with a great deal of detail on pages 9 to 17 of the specification, Finally, Applicants have amended claim 3 and 4 to further define the present invention.

This is not found persuasive for the following reasons:

The Examiner contends that Applicants have not provided a clear definition of the term "coreactant" and, as a result, a person of skill in the art would not know what compounds would or would not infringe on Applicants claimed invention. The law requires that the claims be sufficiently clear that those skilled in the art be able to determine whether a compound is (or is not) within the scope of the claims. In re Mercier, 185 USPQ 774 (C.C.P.A. 1975) (claims sufficiently define an invention so long as one of ordinary skill can determine what subject matter is or is not within the scope of the claims). Here, Applicants have not defined a "coreactant" (see page 6 and also pages 9-17) in sufficiently clear terms that would allow a person of skill in the art to determine whether a compound would or would not fall within the scope of the claims. Applicants use purely functional language to describe a "coreactant" (see page 9, paragraph 2, "The CR [coreactant] ... is a reductant or oxidant capable of intramolecularly providing an electron to or accepting an electron from the EL, so the EL is converted into an excited (i.e., emissive state)") without providing any defined chemical structure resulting in an infinite number of potentially structurally unrelated compounds. The Examiner contends that a person of skill in the art would not know whether a compound would or would not infringe on Applicants claims based on this definition.

It is also noted that Applicants rely on pages 6 and 9-17 of the specification for support of their position; however, Applicants have failed to recite any specific lines and/or sections from those pages that would support their conclusion i.e., Applicants have not shown where any "specific" support may be found. Furthermore, the fact that the "coreactants" are "limited to reactants that can be linked to an ECL label" (see Paper No. 13, page 15, paragraph 4) or limited to compounds that can "undergo oxidation to form a reductant or reduction to form an oxidant" (see newly amended claims) would not help Applicants position because the coreactants are still being described in terms of vague functional language i.e., a person of skill in the art would still not know which compounds would or would not infringe on Applicants claims.

Furthermore, the problem is exacerbated by Applicant's definition of a coreactant on page 6 which includes both precursor species and species which are capable of undergoing transformation to form interactive species (see specification, page 6, paragraph 3, "the term "coreactant" ... encompasses ... species which are capable of undergoing a chemical transformation to form said interactive species or said precursor species"; the Examiner contends that this statement would read on "any" molecule). As the Examiner pointed out in the original rejection, conceivably any compound could fall within Applicants functional language given an infinite number of chemical transformations to change the "precursor species" into the "interactive species."

Finally, the Examiner notes that a claim drawn to a material defined solely in terms of what it can do, or a property thereof, does not particularly point out the claimed invention. Thus, the scope is indefinite. See *ex parte Pulvari* (POBA 1966) 157 USPQ 169.

For ***paragraph D***, Applicants have not provided any specific arguments to refute the original rejection. Consequently, the rejection is hereby maintained.

Accordingly, the rejection under 35 U.S.C. 112, second paragraph, as set forth above (i.e., paragraphs A and D) are hereby maintained.

Claims Rejections - 35 U.S.C. 102

17. Claims 3-4, 10, 12-13 and 18-20, 22, 26-27 and 29-34 are rejected under 35 U.S.C. 102(a) as being anticipated by Liang et al (Liang, P.; Dong, L.; Martin, M. T. "Light Emission from Ruthenium-Labeled Pencillins Signaling Their Hydrolysis by β-Lactamase" *J. Am. Chem. Soc.* **1996**, *118*, 9198-9199).

For ***claim 3-4, 10, 12-13 and 18-20, 22, 26-27 and 29-34***, Liang et al discloses a $Ru(bpy)_3^{2+}$-labeled 6-Aminopenicillanic Acid (Ru-APA) that is hydrolyzed by a β-lactamase (see Liang et al, page 9199, Figures 1 and 2), which reads on all the limitations in claims 3-4, 10, 12-13 and 18-22 because the Ru-APA contains a Ruthenium complex electrochemiluminescent label and a coreactant with a hydrolyzed β-lactam bond.

Response

18. Applicant's arguments directed to the above written description rejection were considered but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicant argues that "Liang et al is not a prior art under 35 U.S.C. § 102(a). The present specification claims priority to June 7, 1995, the filing date of the parent application Serial No. 08/485,419 ... and therefore claims 3-4, 10, 12-13 and 18-22 are entitled to a priority date of June 7, 1995 ... Therefore, the article by Liang et al., published in 1996, is not available as prior art".

This is not found persuasive for the following reasons:

The Examiner contends that claims 3-4, 10, 12-13 and 18-22 are NOT entitled to a June 7, 1995 priority date. As stated by Applicants on page 5 of paper 13, "Applicants submit that claims 9, 11 and 14-16 are supported by parent case U.S.S.N. 08/936,971, and apparently not supported by the disclosures of the other priority applications." Consequently, the generic claims (i.e., claims 3-4) to which claims 9, 11 and 14-17 depend also must not be fully supported because those claims encompass compounds disclosed in claims 9, 11 and 14-17 that are not fully supported. Furthermore, all of the claims (i.e., all of the claims including claim 17) that subsequently depend on these unsupported generic claims (i.e., claims 3-4) also must not be adequately supported including claim 17 (please note that *ipsisima verba* support is not the test for possession). Therefore, the priority of the claims is the date of the parent case 08/936,971 or **September 25, 1997** as stated in the previous Office Action. Therefore, Liang et al can be applied under 35 U.S.C. 102(a) because its publication date is before September 25, 1997 (i.e., it was published in 1996).

Accordingly, the 35 U.S.C. 102 rejection cited above is hereby maintained.

19. Claims 3, 11, 13, 14, 31-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Faulkner, L. R. (Faulkner L. R. "Chemiluminescence from Electron-Transfer Processes" *Methods in Enzymology* (ed. by Marlene A. Deluca) **1978**, *17*, 494-526).

For ***claim 3, 11, 13, 14, 31-34***, Faulkner discloses a compound which comprises an electrochemiluminescent label (anthracene acceptor) linked via a methylene chain to a coreactant (N,N-dimethylaniline donor) which emits electrochemiluminescence when exposed to electrochemical energy (see Faulkner, page 507, third paragraph with structure) ("Annihilation of the ions gives emission from the ***intramolecular*** exciplex"), which anticipates claims 3, 11, 13, 14 because the coreactant (N,N-dimethylaniline) is not an analyte of interest and the coreactant is a tertiary amine.

Response

20. Applicant's arguments directed to the above 35 U.S.C. § 102 rejections were considered but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims.

For the 35 U.S.C. 102(b) rejection under ***Faulkner et al***, Applicant argues that "the compound of Itaya and Toshima would be expected to require oxidation of the luminophore and concurrent reduction of the dimethylamine moiety to provide a strong reductant ... by contrast, the coreactants of amended claim 3 and 4 require a co-reactant that undergoes oxidation to form a reductant or reduction to form an oxidant."

This is not found persuasive for the following reasons:

The Examiner contends that a recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. See *In re Casey*, 152 USPQ 235 (CCPA 1967) and *In re Otto*, 136 USPQ 458, 459 (CCPA 1963). Here, it is not clear what structural limitations would be imposed by Applicant's "intended use" language (see 35 U.S.C. 112, second paragraph rejection above) and, as a result, the additional functional language provided by Applicants has not been given any patentable weight. Furthermore, although Applicants have put forth a mechanism that they believe the compound is undergoing, it does not rule out the possibility that the compound could also undergo the mechanism claimed by Applicant.

In addition, the Examiner argues that the compound disclosed by Faulkner has the same structure as that disclosed by Applicants' specification (e.g., see pages 10-16) and thus must be able to undergo the same types of reactions disclosed by Applicants compounds. For example, Applicants specification states that "some CR species include amines" (see specification, page 10, line 5) and the compound disclosed by Faulkner is a tertiary amine (see 35 USC 102(b) rejection above. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the

burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP § 2112.01.

In addition, the Examiner contends that given an infinite number of chemical transformations (see 35 U.S.C. § 112, second paragraph rejection, above; see also specification, page 6, paragraph 3, "the term "coreactant" ... encompasses ... species which are capable of undergoing a chemical transformation to form said interactive species or said precursor species"; the Examiner contends that this statement would read on "any" molecule) that the compound disclosed by Faulkner is "capable of" being transformed into a compound that would undergo the desired reactions.

Finally, Applicants argue that the Faulker compound does not undergo the "right reaction mechanism" (see Paper No. 13, page 16-17, wherein Applicants argue that the Faulkner compound would not undergo the same mechanistic transformations as Applicants compounds). However, Applicants state that they do not wish to be bound by a theoretical explanation of a reaction mechanism (see specification, page 11, lines -12, "While not wishing to be bound by a theoretical explanation of reaction mechanism, it is postulated that the amine or amine moiety is oxidized by electrochemical energy introduced into the reaction system") and, as a result, Applicants arguments are moot. Furthermore, Applicants are only "postulating" the reaction mechanims, which indicates that they are not even sure how these transformation take place.

Therefore, the Examiner contends that the Faulkner reference still applies.

Accordingly, the above 35 U.S.C. 102 rejection cited above is hereby maintained.

21. Claims 3-4, 10-14 and 19-20, 22, 26-27 and 29-34 are rejected under 35 U.S.C. 102(b) as being anticipated by Massey et al WO 87/06706 (Date of Publication is **November 5, 1987**).

For ***claim 3-4, 10-14 and 19-20, 22, 26-27 and 29-34***, Massey et al teaches a metal containing ECL label linked to a coreactant (see Massey et al, pages 144, 189 and 193 showing a $Ru(bpy)_3$ linked to another $Ru(bpy)_3$ and digoxigenin, $Ru(bpy)_3$ linked to a primary amine, and $Ru(bpy)_3$ linked to a theophylline, respectively), which reads on the limitations in claims 3-4, 10-14 and 19-22. The Digoxigenin conjugate on page 144 meets the limitation of claim 11 wherein "the coreactant is not an analyte of interest" because the coreactant is a $Ru(bpy)_3$ i.e., both the coreactant and the electrochemiluminescent label are $Ru(bpy)_3$ groups, which generate light via the following mechanism $Ru(bpy)_3^{+} + Ru(bpy)_3^{3+} \rightarrow {}^*Ru(bpy)_3^{2+} + Ru(bpy)_3^{2+}$ (see Knight et al, page 884, equation 15) leaving the analyte of interest, digioxigenin or digioxigenin binding compounds, intact. Note: ${}^*Ru(bpy)_3^{2+}$ emits light.

Theophylline and the primary amine shown on pages 189 and 193 would also be considered as coreactants within the definition provide by applicant because it is not clear what compounds fall within this definition (see 112 2nd paragraph rejection above for coreactant).

Response

22. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicant argues that **[1]** digoxigenin and theophylline are "the analytes of interest not the coreactants" (see Paper 13, page 18, paragraph 2), **[2]** "digoxigenin and theophylline do not play a role in the actual emission of ECL and can not be considered a "coreactant" (see Paper 13, page 18, paragraph 2), **[3]** Massey ('706) does not teach or suggest that one of the Ru(bpy)3 molecules may work as a coreactant for another Ru(bpy)3 molecule ... it appears that both Ru(bpy)3 molecules are the same oxidation state ... and thus do not result in an ECL label/coreactant pair, **[4]** "Massey ('706) relates to complexes where both the ECL label Ru(bpy)3 molecules are linked to an analyte of interest (digoxigenin) and not to each other" (see Paper 13, page 18, paragraph 4).

This is not found persuasive for the following reasons:

The Examiner contends that **[1]** the specification and claims do not limit the possibility that the "analyte" and the "coreactant" can be the same molecule, **[2]** the definition of "coreactant" also include compounds that are capable after chemical transformation of participating in an ECL reaction. Applicants have not shown that digoxigenin and theophylline could not participate in an ECL reaction given an infinite number of chemical transformations to a more appropriate structure (see specification, page 6, paragraph 3, "the term "coreactant" ... encompasses ... species which are capable of undergoing a chemical transformation to form said interactive species or said precursor species"; the Examiner contends that this statement would read on "any" molecule; see also 35 U.S.C. 112, second paragraph rejection above), **[3]** Applicants' definition of coreactant is very broad and would include molecules that are capable of functioning as coreactants after they have been chemically transformed (see specification, page 6, paragraph 3, "the term "coreactant" ... encompasses ... species which are capable of

undergoing a chemical transformation to form said interactive species or said precursor species"; the Examiner contends that this statement would read on "any" molecule; see also 35 U.S.C. 112, second paragraph rejection above). The Examiner argues that given an unlimited number of chemical transformations the $Ru(bpy)_3$ could function as a coreactant even assuming arguendo that it cannot in its current form. **[4]** As stated above, the specification and claims do not limit the possibility that the "analyte" and the "coreactant" can be the same molecule and the definition of "coreactant" is very broad reading on "any" compound (see specification, page 6, paragraph 3, "the term "coreactant" ... encompasses ... species which are capable of undergoing a chemical transformation to form said interactive species or said precursor species"; the Examiner contends that this statement would read on "any" molecule; see also 35 U.S.C. 112, second paragraph rejection above).

Accordingly, the 35 U.S.C. 102 rejection cited above is hereby maintained.

23. Claims 3-4, 10-12, 13-14 and 19-20, 22, 26-27 and 29-34 are rejected under 35 U.S.C. 102(e) as being anticipated by Massey et al (US Pat No. 5,591,581) (Date of Patent is **January 7, 1997**; Date Filed is **April 15, 1994**).

Claims ***3-4, 10-12, 13-14, 19-20, 22, 26-27 and 29-34*** are directed to a compound which is a ruthenium containing ECL labile linked via an amide bond to a coreactant which includes amines and teriary amines wherein the coreactant can be a strong oxidant or a strong reductant.

For claims, 3-4, 10-12, 13-14, 19-20, 22, 26-27 and 29-34 Massey et al discloses electrochemiluminescent labels with a coordinated Re atom linked to numerous compounds 'B'

where B can be peptides, nucleic acids, polysaccharides, alkaloids, steroids, vitamins, amino acids or non-biological polymers (see Massey et al, claim 1). Massey also teaches amines linked to ECL labels (see Massey et al, column 15, lines 1-15; column 30, lines 38-column 31 line 37). Note that proteins have amine groups as well e.g., lysine side chains, etc. and well as alkaloids, polysaccharides that contain amino pentose and hexose units, and amino steroids, which reads on claims 3-4, 10-12, 13-14 and 19-22.

Response

24. Applicant's arguments directed to the above 35 U.S.C. § 102 rejection were fully considered but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicants argue that **[1]** "Massey patent does not disclose B as a "coreactant" or a precursor species or species which undergoes a chemical transformation and thereafter interacts with an ECL label to produce ECL" (see Paper 13, page 19, paragraph 2), **[2]** "the amines cited by the Examiner in the '561 patent ... are part of the compound and are not disclosed as coreactants" (see Paper 13, page 19, paragraphs 3-4).

This is not found persuasive for the following reasons:

The Examiner contends that **[1]** the Massey patent does not have to disclose a coreactant that "undergoes a chemical transformation and thereafter interacts with an ECL label" because Applicants definition includes only compounds that are "capable of" undergoing the chemical transformation (see specification page 6, paragraph 3). Furthermore, although the claims are

interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). **[2]** As stated above, the specification and claims do not limit the possibility that the "analyte" and the "coreactant" can be the same molecule and the definition of "coreactant" is very broad reading on "any" compound (see specification, page 6, paragraph 3, "the term "coreactant" ... encompasses ... species which are capable of undergoing a chemical transformation to form said interactive species or said precursor species"; the Examiner contends that this statement would read on "any" molecule; see also 35 U.S.C. 112, second paragraph rejection above).

Accordingly, the 35 U.S.C. 102 rejection cited above is hereby maintained.

25. Claims 3-4, 10-12, 13-14, 19-20, 22, 26-27 and 29-34 are rejected under 35 U.S.C. 102(f) as being unpatentable over Massey et al (US Pat No. 5,591,581) (Date of Patent is **January 7, 1997**; Date Filed is **April 15, 1994**). The claimed subject matter appears to have been invented by Massey et al.

Claims ***3-4, 10-12, 13-14, 19-20, 22, 26-27 and 29-34*** are directed to an invention not patentably distinct from claims 1-6 and 20 of commonly assigned 5,591,581. Specifically the applicant's are directed to the teachings of Massey et al '581 as applied under 35 USC 102(e) *supra*.

Response

26. Applicant's arguments directed to the above 35 U.S.C. § 102(g) rejection were found persuasive and the rejection is hereby withdrawn. Applicant's arguments directed to the above 35 U.S.C. § 102(f) rejection were fully considered but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicant argues that "the inventions were commonly owned at the time of the invention of this application" (see Paper No. 13, page 20, paragraph 1.

This is not found persuasive for the following reasons:

The Examiner contends that common ownership can be used to successfully overcome a 35 U.S.C. § 102(g) rejection, but not a 35 U.S.C. § 102(f) rejection as made in the present case. Since the U.S. Patent and Trademark Office normally will not institute an interference between applications or a patent and an application of common ownership (see MPEP § 2302), the assignee is required to state which entity is the prior **"inventor"** of the conflicting subject matter. A terminal disclaimer has no effect in this situation since the basis for refusing more than one patent is priority of invention under 35 U.S.C. 102(f) or (g) and not an extension of monopoly. Here, Applicants have not indicated the inventor of the conflicting subject matter.

Accordingly, the 35 U.S.C. 102(f) rejection cited above is hereby maintained.

Failure to comply with this requirement will result in a holding of abandonment of this application.

Claim Rejections - 35 USC § 103

27. Claims 3-4, 9-20, 22 and 26-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knight et al (Knight, A. W.; Greenway, G. M. "Occurrence, Mechanisms and Analytical Applications of Electrogenerated Chemiluminescence" *Analyst* 1994, *119*, 879-890) in view of Faulkner, L. R. (Faulkner L. R. "Chemiluminescence from Electron-Transfer Processes" *Methods in Enzymology* (ed. by Marlene A. Deluca) 1978, *17*, 494-526).

Knight et al teaches a large number of electrochemiluminescent compounds including $Ru(bpy)_3^{2+}$ complexes (see Knight et al, page 880, Table I, ruthenium complexes), which reads on claims 3-4, 9-19, 21-22. Knight also teaches a large number of coreactants including trialkylamines, NADH (see Knight et al, page 882, Table II, references 67, 79), which reads on claims 3-4, 9-17, 19, 21-22. Knight et al also teaches that ECL/coreactants can be used to detect biomolecules including amino acids, peptides an proteins (see Knight et al, page 884, column 2, line 12) and DNA (see Knight et al page 883, Table II, reference 82), which reads on claims 10 and 12.

The claimed invention differs from the prior art teaching of Knight et al by reciting the advantages to be gained by linking an EL with a CR. Knight et al does not teach the advantage of linking an EL with a CR. However, Faulkner does teach the advantages to be gained by linking an EL with a CR by describing the work of Itaya and Toshima which provides an example of an anthracene linked to an N,N-dimethylaniline.

It would have been prima facia obvious to one having ordinary skill in the art at the time the invention was made to combine the teachings of Knight et al with Faulkner as outlined above

because both papers disclose compounds for electrogenerated chemiluminescence (i.e., each paper encompasses overlapping subject matter e.g., both papers show the use of anthracene and tertiary aromatic amines in electrogenerated chemiluminescence).

Furthermore, one of ordinary skill in the art would have been motivated to use the EL and CR compounds as taught by Knight with a linker to join the EL with the CR as taught by Faulkner because Faulkner specifically states the "advantages" of linking an EL to a CR (see Faulkner, pages 507-508) ("The linked systems [provide] an unusually efficient exciplex emission ... Note also that [the linked exciplex] is stabilized in a polar medium, rather than being destabilized as true exciplexes are. It is not surprising [i.e., it's obvious] that its chemiluminescence is very much brighter than that from the usual exciplex systems in polar solvents). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Faulkner et al shows a working example of applicant's invention e.g., the anthracene linked to the N,N-dimethylaniline via a methylene chain (see Faulnker, page 507, third paragraph).

Response

28. Applicant's arguments directed to the above 35 U.S.C. § 103(a) rejection were considered but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version in Paper No. 2 to more clearly address applicants' newly amended and/or added claims.

Applicant argues that "Faulkner LR does not compensate for the deficiencies of Knight et al because Faulkner does not teach or suggest ... that the coreactant of the cited compound can undergo oxidation to form a reductant, or reduction to form an oxidant".

This is not found persuasive for the following reasons:

The Examiner contends that the combined teachings of Faulkner LR and Kinght et al teach compounds that fall within the scope of Applicants claimed invention i.e., tertiary amines and, as a result, these compounds would inherently have these properties. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). See MPEP § 2112.01.

Furthermore, Applicants state in further state in the specification that tey do not wish to be bound by theoretical explanation of reaction mechanism (see specification, page 11, paragraph 1, "While not wishing to be bound by a theoretical explanation of reaction mechanism, it is postulated that the amine or amine moiety is oxidized by electrochemical energy introduced into the reaction system") and, as a result, it is not clear what further limitations these mechanistic requirements would have (see 35 U.S.C. 112, second paragraph rejections below). Consequently, these amendments have not been given any patentable weight.

Accordingly, the 35 U.S.C. § 103(a) rejection cited above is hereby maintained.

Double Patenting

29. Claims 3-4, 9-20, 22 and 26-34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 and 19-20 of U.S. Patent No. 5, 591,581. Although the conflicting claims are not identical, they are not patentably distinct from each other.

Claims 3 and 4 are directed to a compound which is a metal containing ECL labile linked to a coreactant because Massey et al discloses electrochemiluminescent labels with a coordinated Re atom linked to numerous compounds (B) where B can be peptides, nucleic acids, polysaccharides, alkaloids, steroids, vitamins, amino acids or non-biological polymers (see claim 1 for example). As a coreactant includes precursor species and species which upon the chemical transormation which result in species which can interact with the label to induce electrochemiluminescence Massey et al anticipates claims 3-4.

In addition, U.S. Patent No. 5,591,581 also amines linked to ECL labels.

30. Claims 3-4, 9-20, 22 and 26-34 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,643,713. Although the conflicting claims are not identical, they are not patentably distinct from each other.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: Compounds which comprise an electrochemiluminescent label linked to a coreactant

as set forth in claims 3 and 4 of the instant application are substantially identical if not identical to those set forth in US 5,643,713, claims 1 and 6, although recited in slightly different language or by structure. One of ordinary skill in the art would recognize that the coreactant as recited in claims of the instant application are equivalent to the chemically transformable first compound as set forth in claim 1 of the 5,643,713 patent and have the properties recited in section I of the claim and undergo the reaction as set forth in section II of the claim.

Furthermore, there is no apparent reason why applicants were prevented from presenting claims corresponding to those of the instant application during prosecution of the application that matured into a patent. See In re Schneller, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

In addition to the teachings previously recited note that claim 6 recites an aromatic coreactant.

Response

31. Applicant's arguments directed to the above double patenting rejection were fully considered but were not deemed persuasive for the following reasons. Please note that the above rejection has been modified from it original version to more clearly address applicants' newly amended and/or added claims and/or arguments.

Applicant argues that [a] "the present claims are not rendered obvious in view of claims of the '581 patent ... the present claims relate to compounds comprising ECL labels linked to co-reactants, wherein the compounds are capable of emitting ECL. The claims of the '581 Massey

patent do not" (see Paper No. 13, pages 21-22), [b] "Applicants will consider the submission of the terminal disclaim upon allowance of the claims" (see Paper No. 13, page 22).

This is not found persuasive for the following reasons:

The Examiner contends that [1] the '581 patent does read on Applicants invention (see 35 U.S.C. § 102 rejection above under Massey et al, [2] the Examiner will consider Applicants arguments when the terminal diclaimer is filed.

Accordingly, the double patenting rejection(s) cited above are hereby maintained.

New Rejections

Claims Rejections - 35 U.S.C. 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

32. Claims 3-4, 9-20, 22 and 26-34 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 3-4, 9-20, 22 and 26-34 recite both a "product" and a "method of use" (see 35 U.S.C. 112, second paragraph rejection below). However, Applicants may only obtain "a" patent i.e., one (1) patent for a "product" OR a "method", not a product/method of use "hybrid" and, as a result, claims 3-4 and all dependent claims are rejected under 35 U.S.C. 101.

Claims Rejections - 35 U.S.C. 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

33. Claims 3-4, 9-20, 22 and 26-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention. This is a new matter rejection.

Claim(s) 3-4 were amended in Paper No. 13 to recite "wherein said coreactant undergoes oxidation to form a reduction or reduction to form an oxidant." However, the specification does not support these amendment(s) because the specification explicitly states that the scope of the invention is not to be bound by a theoretical explanation of the reaction mechanism (see specification page 11, lines 1-2) and Applicants current amendments would fall within the scope of that statement because the reduction and/or oxidation of the coreactant defines Applicants postulated mechanism by which the ECL reaction occurs (see specification, pages 10-11). Therefore, Applicants were not is possession of the smaller amended subgenus. Therefore, claims 3-4 and all dependent claims are rejected as new matter.

Furthermore, the Examiner cannot find support for [1] "a combination thereof" of the linkers listed in claim 28, [2] "combinations thereof" of linkers listed in claim 29. If applicant believes this rejection is in error, applicant must disclose where in the specification support for these amendments can be found. Therefore, claim 28-29 and all-dependent claims represent new matter.

Claims Rejections - 35 U.S.C. 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

34. Claims 3-4, 9-20, 22 and 26-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. For **claims 3-4**, the phrases "wherein said coreactant undergoes oxidation to form a reductant or rejection to form an oxidant" is vague and indefinite. For example, it is not clear whether Applicant is claiming a "product" or a "method of using" said product (see claims 3-4 wherein Applicants claim a compound (i.e., a label linked to a coreactant) and also claims method steps (i.e., "said coreactant undergoes [present tense] oxidation to form a reductant or reduction to form an oxidant"). Furthermore, if Applicant intends for the compounds to just have the "ability" to undergo the transformation, the Examiner contends that the functional language is indefinite. A claim to a material defined solely in terms of what it can do, or a property thereof, does not particularly point out the claimed invention. Thus, the scope is indefinite. See *ex parte Pulvari* (POBA 1966) 157 USPQ 169. Therefore, claims 3-4 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

B. Claim(s) **32-33** are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter

which applicant regards as the invention. The terms "reductant precursor" and "oxidant precursor" in claim 32-22 is a relative term which renders the claim indefinite. The term "precursor" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. There is no identified limit to how much the structure can deviate from the claimed oxidant and/or reductant and still be considered a precursor. Consequently, the metes and bounds of the claimed invention cannot be determined and claims 32-33 and all dependent claims are rejected under 35 U.S.C. 112, second paragraph.

Claim Rejections - 35 USC § 103

35. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

36. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

37. Claims 3-4, 9-20, 22 and 26-34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Knight et al (Knight, A. W.; Greenway, G. M. "Relationship between structural attributes and observed electrogenerated chemiluminescence (ECL) activity of tertiary amines as potential analytes for the tris(2,2-bipyridine)ruthenium(II) ECL Reaction" *Analyst* 1996, *121*, 101R-106R) in view of Faulkner, L. R. (Faulkner L. R. "Chemiluminescence from Electron-Transfer Processes" *Methods in Enzymology* (ed. by Marlene A. Deluca) 1978, *17*, 494-526).

Knight et al teaches electrochemiluminescent compounds including $Ru(bpy)_3^{2+}$ complexes (see Knight et al, page 101R, abstract). Knight also teaches coreactants including tertiary amines like tripropylamine (see Knight et al, page 103R, column 2, first paragraph). Knight et al also teaches that ECL/coreactants can be used to detect biomolecules including pharmaceuticals, amino acids and antibiotics (see Knight et al, page 101R, column 2, paragraph 3,). Knight et al further teaches Applicants reaction mechanism wherein the coreactant i.e., the tertiary amine undergoes oxidation or reduction to form a reductant or oxidant, respectively (see Knight et al, page 101R, column 2, paragraph 3; see also 102R, reaction mechanism section).

The claimed invention differs from the prior art teaching of Knight et al by reciting the advantages to be gained by linking an EL with a CR. Knight et al does not teach the advantage of linking an EL with a CR. However, Faulkner does teach the advantages to be gained by linking an EL with a CR by describing the work of Itaya and Toshima which provides an example of an anthracene linked to an N,N-dimethylaniline.

It would have been prima facia obvious to one having ordinary skill in the art at the time the invention was made to combine the teachings of Knight et al with Faulkner as outlined above because both papers disclose compounds for electrogenerated chemiluminescence (i.e., each paper encompasses overlapping subject matter e.g., both papers show the use of an EL and a CR in electrogenerated chemiluminescence).

Furthermore, one of ordinary skill in the art would have been motivated to use the EL and CR compounds as taught by Knight et al (i.e., the $Ru(bpy)_3^{2+}$ complexes with tripropylamine) with a linker to join the EL with the CR as taught by Faulkner because Faulkner specifically states the "advantages" of linking an EL to a CR (see Faulkner, pages 507-508) ("The linked systems [provide] an unusually efficient exciplex emission ... Note also that [the linked exciplex] is stabilized in a polar medium, rather than being destabilized as true exciplexes are. It is not surprising [i.e., it's obvious] that its chemiluminescence is very much brighter than that from the usual exciplex systems in polar solvents). Furthermore, one of ordinary skill in the art would have reasonably expected to be successful because Faulkner et al shows a working example of applicant's invention e.g., the anthracene linked to the N,N-dimethylaniline via a methylene chain (see Faulnker, page 507, third paragraph) and Knight et al teaches that tripropylamine would be an excellent candidate to "link" to the $Ru(bpy)_3^{2+}$ (see Knight et al, page 103R, column 2, paragraph 1, "Tripropylamine has proved to be perhaps the most efficient amine for this ECL reaction, and is commonly used as a standard by which to compare the ECL activity of other amines"; please note that Applicants preferred embodiments are drawn to teriary amines including tripropylamine "linked" to $Ru(bpy)_3^{2+}$).

Conclusion

Applicant's amendment necessitated any new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jon D. Epperson, Ph.D. whose telephone number is (703) 308-2423. The examiner can normally be reached on Monday-Thursday from 9:30 to 7:00 and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang, can be reached on (703) 306-3217. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Jon D. Epperson, Ph.D.
May 27, 2003

BENNETT CELSA
PRIMARY EXAMINER